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Applicant: Taylor *et al.*
Serial No.: 09/898,779
Filed: July 3, 2001
For: **GENETIC TEST TO DETERMINE NON-RESPONSIVENESS TO STATIN DRUG TREATMENT**

Art Unit: 1655
Examiner: Goldberg, J.A.

RESPONSE TO OFFICE ACTION

Assistant Commissioner for Patents
Washington, D. C. 20231

CERTIFICATE OF MAILING
I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS FIRST CLASS MAIL IN AN ENVELOPE ADDRESSED TO THE ASSISTANT COMMISSIONER FOR PATENTS WASHINGTON, D. C. 20231, ON APRIL 25, 2002 (DATE)
BY ANN WEISS
APRIL 25, 2002 (DATE OF SIGNATURE)

Dear Sir or Madam:

This is in response to the Office Action mailed January 25, 2002, for the above-captioned patent application. This response is submitted on or before April 25, 2002. In connection with the above-captioned application, the Examiner is respectfully requested to consider the following amendment and remarks.

AMENDMENTS

A VERSION WITH MARKINGS TO SHOW CHANGES MADE is found beginning at page 22, after Applicant's Remarks.

In the Specification:

At page 1, lines 1-2, please delete the title and insert therefor the following new title:

--OLIGONUCLEOTIDE PRIMER SEQUENCES, PRIMER SETS, AND GENETIC TESTING KITS FOR LIPOPROTEIN LIPASE GENE ALLELES--.

At page 1, line 3, between the title and the Background of the Invention section, please delete the paragraph and insert therefor the following paragraph:

B2 --This application is a continuation of U.S. Serial No. 09/347,114, filed on July 2, 1999, which issued as U.S. Patent No. 6,297,014, on October 2, 2001.--.

In the Claims:

Please cancel Claims 82 and 83, without prejudice. Please amend Claims 84-86, 89, 91-93, and 95-102, and add new Claims 103-117, as follows.

84. (Amended) An oligonucleotide primer for detecting a genetic predisposition for non-responsiveness to statin drug treatment in a human, said primer having a nucleotide sequence consisting of 5'-GCA TCT GCC TTC AGC TAG ACA TTG-3' (SEQ. ID. NO. 1).

B3 85. (Amended) An oligonucleotide primer for detecting a genetic predisposition for non-responsiveness to statin drug treatment in a human, said primer having a nucleotide sequence consisting of 5'-TCT TCC AGA AGG GTG AGA TTC CAA-3' (SEQ. ID. NO.:2).

86. (Twice Amended) An oligonucleotide primer for detecting a genetic predisposition for non-responsiveness to statin drug treatment in a human, said primer having a nucleotide sequence consisting of (SEQ. ID. NO.:1), (SEQ. ID. NO.:2), (SEQ. ID. NO.:3), (SEQ. ID. NO.:4), (SEQ. ID. NO.:5), (SEQ. ID. NO.:6), (SEQ. ID. NO.:7), (SEQ. ID. NO.:8), (SEQ. ID. NO.:9), (SEQ. ID. NO.:10), (SEQ. ID. NO.:11), (SEQ. ID. NO.:12), (SEQ. ID. NO.:13), (SEQ. ID. NO.:14), (SEQ. ID. NO.:15), (SEQ. ID. NO.:16), (SEQ. ID. NO.:17), (SEQ. ID. NO.:18), (SEQ. ID. NO.:19), (SEQ. ID. NO.:20), (SEQ. ID. NO.:21), (SEQ. ID. NO.:22), (SEQ. ID. NO.:23), (SEQ. ID. NO.:24), (SEQ. ID. NO.:25), (SEQ. ID. NO.:26),

(SEQ. ID. NO.:27), (SEQ. ID. NO.:28), (SEQ. ID. NO.:29), (SEQ. ID. NO.:30), (SEQ. ID. NO.:31), (SEQ. ID. NO.:32),(SEQ. ID. NO.:35), (SEQ. ID. NO.:36), (SEQ. ID. NO.:37), (SEQ. ID. NO.:38), (SEQ. ID. NO.:39), (SEQ. ID. NO.:40), (SEQ. ID. NO.:41), (SEQ. ID. NO.:42), (SEQ. ID. NO.:43), (SEQ. ID. NO.:44), (SEQ. ID. NO.:45),(SEQ. ID. NO.:46), (SEQ. ID. NO.:47), (SEQ. ID. NO.:48), (SEQ. ID. NO.:49), (SEQ. ID. NO.:50), (SEQ. ID. NO.:51), (SEQ. ID. NO.:52), (SEQ. ID. NO.:53), (SEQ. ID. NO.:54), (SEQ. ID. NO.:55), (SEQ. ID. NO.:56), (SEQ. ID. NO.:57), (SEQ. ID. NO.:58), (SEQ. ID. NO.:59), (SEQ. ID. NO.:60), (SEQ. ID. NO.:61), (SEQ. ID. NO.:62), (SEQ. ID. NO.:63), (SEQ. ID. NO.:64), (SEQ. ID. NO.:65), (SEQ. ID. NO.:66), (SEQ. ID. NO.:67), (SEQ. ID. NO.:68), (SEQ. ID. NO.:69), (SEQ. ID. NO.:70), (SEQ. ID. NO.:71), (SEQ. ID. NO.:72), (SEQ. ID. NO.:73), (SEQ. ID. NO.:74), (SEQ. ID. NO.:75), (SEQ. ID. NO.:76), (SEQ. ID. NO.:77), (SEQ. ID. NO.:78), or (SEQ. ID. NO.:79).

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89. (Twice Amended) An oligonucleotide primer for detecting a genetic predisposition for non-responsiveness to statin drug treatment in a human, said primer having a nucleotide sequence consisting of (SEQ. ID. NO.:82), (SEQ. ID. NO.:83), (SEQ. ID. NO.:84), (SEQ. ID. NO.:85), (SEQ. ID. NO.:86), (SEQ. ID. NO.:88), (SEQ. ID. NO.:89), (SEQ. ID. NO.:90), or (SEQ. ID. NO.:92).

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91. (Twice Amended) An oligonucleotide primer for detecting a genetic predisposition for non-responsiveness to statin drug treatment in a human, said primer having a nucleotide sequence consisting of (SEQ. ID. NO.:95), (SEQ. ID. NO.:96), (SEQ. ID. NO.:97), (SEQ. ID. NO.:98), (SEQ. ID. NO.:99), (SEQ. ID. NO.:100), (SEQ. ID. NO.:101), (SEQ. ID. NO.:102), (SEQ. ID. NO.:103), (SEQ. ID. NO.:104), (SEQ. ID. NO.:105), or (SEQ. ID. NO.:106).

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92. (Twice Amended) An oligonucleotide primer set for detecting a genetic predisposition for non-responsiveness to statin drug treatment in a human, said primer set having a reverse primer having a nucleotide sequence consisting of

5'-GCA TCT GCC TTC AGC TAG ACA TTG-3' (SEQ. ID. NO.:1); and a forward primer having a nucleotide sequence consisting of 5'-TCT TCC AGA AGG GTG AGA TTC CAA-3' (SEQ. ID. NO.:2).

93. (Twice Amended) An oligonucleotide primer set for detecting a genetic predisposition for non-responsiveness to statin drug treatment in a human, having a forward primer having a nucleotide sequence consisting of (SEQ. ID. NO.:2), (SEQ. ID. NO.:3), (SEQ. ID. NO.:4), (SEQ. ID. NO.:5), (SEQ. ID. NO.:6), (SEQ. ID. NO.:7), (SEQ. ID. NO.:8), (SEQ. ID. NO.:9), (SEQ. ID. NO.:11), (SEQ. ID. NO.:12), (SEQ. ID. NO.:13), (SEQ. ID. NO.:14), (SEQ. ID. NO.:15), (SEQ. ID. NO.:16), (SEQ. ID. NO.:17), (SEQ. ID. NO.:18), (SEQ. ID. NO.:19), (SEQ. ID. NO.:20), (SEQ. ID. NO.:21), (SEQ. ID. NO.:22), (SEQ. ID. NO.:23), (SEQ. ID. NO.:36), (SEQ. ID. NO.:37), (SEQ. ID. NO.:38), (SEQ. ID. NO.:39), (SEQ. ID. NO.:43), (SEQ. ID. NO.:45), (SEQ. ID. NO.:47), (SEQ. ID. NO.:48), (SEQ. ID. NO.:49), (SEQ. ID. NO.:50), (SEQ. ID. NO.:53), (SEQ. ID. NO.:54), (SEQ. ID. NO.:58), (SEQ. ID. NO.:59), (SEQ. ID. NO.:60), (SEQ. ID. NO.:61), (SEQ. ID. NO.:65)(SEQ. ID. NO.:66), (SEQ. ID. NO.:67), (SEQ. ID. NO.:68), (SEQ. ID. NO.:69), (SEQ. ID. NO.:70), (SEQ. ID. NO.:71), (SEQ. ID. NO.:72), (SEQ. ID. NO.:75), (SEQ. ID. NO.:76), (SEQ. ID. NO.:77), or (SEQ. ID. NO.:79);

and having a reverse primer having a nucleotide sequence consisting of (SEQ. ID. NO.:1),(SEQ. ID. NO.:10), (SEQ. ID. NO.:24), (SEQ. ID. NO.:25), (SEQ. ID. NO.:26), (SEQ. ID. NO.:27), (SEQ. ID. NO.:28), (SEQ. ID. NO.:29), (SEQ. ID. NO.:30), (SEQ. ID. NO.:31), (SEQ. ID. NO.:32), (SEQ. ID. NO.:35), (SEQ. ID. NO.:40), (SEQ. ID. NO.:41), (SEQ. ID. NO.:42), (SEQ. ID. NO.:44), (SEQ. ID. NO.:46), (SEQ. ID. NO.:51), (SEQ. ID. NO.:52), (SEQ. ID. NO.:55), (SEQ. ID. NO.:56), (SEQ. ID. NO.:57), (SEQ. ID. NO.:62), (SEQ. ID. NO.:63), (SEQ. ID. NO.:64), (SEQ. ID. NO.:73), (SEQ. ID. NO.:74), or (SEQ. ID. NO.:78).

95. (Twice Amended) An oligonucleotide primer set for detecting a genetic predisposition for non-responsiveness to statin drug treatment in a human, having a forward primer having a nucleotide sequence consisting of (SEQ. ID. NO.:82), (SEQ. ID. NO.:86), (SEQ. ID. NO.:88), (SEQ. ID. NO.:90), or (SEQ. ID. NO.:92);

and having a reverse primer having a nucleotide sequence consisting of (SEQ. ID. NO.:83), (SEQ. ID. NO.:84), (SEQ. ID. NO.:85), or (SEQ. ID. NO.:89).

96. (Twice Amended) An oligonucleotide primer set for detecting a genetic predisposition for non-responsiveness to statin drug treatment in a human, having a forward primer having a nucleotide sequence consisting of (SEQ. ID. NO.:95),(SEQ. ID. NO.:98), (SEQ. ID. NO.:99), (SEQ. ID. NO.:101), (SEQ. ID. NO.:102), (SEQ. ID. NO.:104), or (SEQ. ID. NO.:106);

and having a reverse primer having a nucleotide sequence consisting of (SEQ. ID. NO.:96), (SEQ. ID. NO.:97), (SEQ. ID. NO.:100), (SEQ. ID. NO.:103), or (SEQ. ID. NO.:105).

97. (Twice Amended) A genetic testing kit comprising a primer having a nucleotide sequence consisting of (SEQ. ID. NO.:1), (SEQ. ID. NO.:2), (SEQ. ID. NO.:3), (SEQ. ID. NO.:4), (SEQ. ID. NO.:5), (SEQ. ID. NO.:6), (SEQ. ID. NO.:7), (SEQ. ID. NO.:8), (SEQ. ID. NO.:9), (SEQ. ID. NO.:10), (SEQ. ID. NO.:11), (SEQ. ID. NO.:12), (SEQ. ID. NO.:13), (SEQ. ID. NO.:14), (SEQ. ID. NO.:15), (SEQ. ID. NO.:16), (SEQ. ID. NO.:17), (SEQ. ID. NO.:18), (SEQ. ID. NO.:19), (SEQ. ID. NO.:20), (SEQ. ID. NO.:21), (SEQ. ID. NO.:22), (SEQ. ID. NO.:23), (SEQ. ID. NO.:24), (SEQ. ID. NO.:25), (SEQ. ID. NO.:26), (SEQ. ID. NO.:27), (SEQ. ID. NO.:28), (SEQ. ID. NO.:29), (SEQ. ID. NO.:30), (SEQ. ID. NO.:31), (SEQ. ID. NO.:32), (SEQ. ID. NO.:35), (SEQ. ID. NO.:36), (SEQ. ID. NO.:37), (SEQ. ID. NO.:38), (SEQ. ID. NO.:39), (SEQ. ID. NO.:40), (SEQ. ID. NO.:41), (SEQ. ID. NO.:42), (SEQ. ID. NO.:43), (SEQ. ID. NO.:44), (SEQ. ID.

NO.:45),(SEQ. ID. NO.:46), (SEQ. ID. NO.:47), (SEQ. ID. NO.:48), (SEQ. ID. NO.:49), (SEQ. ID. NO.:50), (SEQ. ID. NO.:51), (SEQ. ID. NO.:52), (SEQ. ID. NO.:53), (SEQ. ID. NO.:54), (SEQ. ID. NO.:55), (SEQ. ID. NO.:56), (SEQ. ID. NO.:57), (SEQ. ID. NO.:58), (SEQ. ID. NO.:59), (SEQ. ID. NO.:60), (SEQ. ID. NO.:61), (SEQ. ID. NO.:62), (SEQ. ID. NO.:63), (SEQ. ID. NO.:64), (SEQ. ID. NO.:65), (SEQ. ID. NO.:66), (SEQ. ID. NO.:67), (SEQ. ID. NO.:68), (SEQ. ID. NO.:69), (SEQ. ID. NO.:70), (SEQ. ID. NO.:71), (SEQ. ID. NO.:72), (SEQ. ID. NO.:73), (SEQ. ID. NO.:74), (SEQ. ID. NO.:75), (SEQ. ID. NO.:76), (SEQ. ID. NO.:77), (SEQ. ID. NO.:78), or (SEQ. ID. NO.:79); and

instructions for using the primer to detect a genetic predisposition in a human subject for non-responsiveness to treatment with a statin drug selected from the group consisting of lovastatin, pravastatin, and simvastatin.

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98. (Twice Amended) A genetic testing kit comprising:

a primer having a nucleotide sequence consisting of (SEQ. ID. NO.:82), (SEQ. ID. NO.:83), (SEQ. ID. NO.:84), (SEQ. ID. NO.:85), (SEQ. ID. NO.:86), (SEQ. ID. NO.:88), (SEQ. ID. NO.:89), (SEQ. ID. NO.:90), or (SEQ. ID. NO.:92); and

instructions for using the primer to detect a genetic predisposition in a human subject for non-responsiveness to treatment with a statin drug selected from the group consisting of lovastatin, pravastatin, and simvastatin.

99. (Twice Amended) A genetic testing kit comprising:

a primer having a nucleotide sequence consisting of (SEQ. ID. NO.:95), (SEQ. ID. NO.:96), (SEQ. ID. NO.:97), (SEQ. ID. NO.:98), (SEQ. ID. NO.:99), (SEQ. ID. NO.:100), (SEQ. ID. NO.:101), (SEQ. ID. NO.:102), (SEQ. ID. NO.:103), (SEQ. ID. NO.:104), (SEQ. ID. NO.:105), or (SEQ. ID. NO.:106); and

instructions for using the primer to detect a genetic predisposition in a human subject for non-responsiveness to treatment with a statin drug selected from the group consisting of lovastatin, pravastatin, and simvastatin.

100. (Twice Amended) A genetic testing kit comprising:

a forward primer having a nucleotide sequence consisting of (SEQ. ID. NO.:2), (SEQ. ID. NO.:3), (SEQ. ID. NO.:4), (SEQ. ID. NO.:5), (SEQ. ID. NO.:6), (SEQ. ID. NO.:7), (SEQ. ID. NO.:8), (SEQ. ID. NO.:9), (SEQ. ID. NO.:11), (SEQ. ID. NO.:12), (SEQ. ID. NO.:13), (SEQ. ID. NO.:14), (SEQ. ID. NO.:15), (SEQ. ID. NO.:16), (SEQ. ID. NO.:17), (SEQ. ID. NO.:18), (SEQ. ID. NO.:19), (SEQ. ID. NO.:20), (SEQ. ID. NO.:21), (SEQ. ID. NO.:22), (SEQ. ID. NO.:23), (SEQ. ID. NO.:36), (SEQ. ID. NO.:37), (SEQ. ID. NO.:38), (SEQ. ID. NO.:39), (SEQ. ID. NO.:43), (SEQ. ID. NO.:45), (SEQ. ID. NO.:47), (SEQ. ID. NO.:48), (SEQ. ID. NO.:49), (SEQ. ID. NO.:50), (SEQ. ID. NO.:53), (SEQ. ID. NO.:54), (SEQ. ID. NO.:58), (SEQ. ID. NO.:59), (SEQ. ID. NO.:60), (SEQ. ID. NO.:61), (SEQ. ID. NO.:65), (SEQ. ID. NO.:66), (SEQ. ID. NO.:67), (SEQ. ID. NO.:68), (SEQ. ID. NO.:69), (SEQ. ID. NO.:70), (SEQ. ID. NO.:71), (SEQ. ID. NO.:72), (SEQ. ID. NO.:75), (SEQ. ID. NO.:76), (SEQ. ID. NO.:77), or (SEQ. ID. NO.:79);

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a reverse primer having a nucleotide sequence consisting of (SEQ. ID. NO.:1),(SEQ. ID. NO.:10), (SEQ. ID. NO.:24), (SEQ. ID. NO.:25), (SEQ. ID. NO.:26), (SEQ. ID. NO.:27), (SEQ. ID. NO.:28), (SEQ. ID. NO.:29), (SEQ. ID. NO.:30), (SEQ. ID. NO.:31), (SEQ. ID. NO.:32), (SEQ. ID. NO.:35), (SEQ. ID. NO.:40), (SEQ. ID. NO.:41), (SEQ. ID. NO.:42), (SEQ. ID. NO.:44), (SEQ. ID. NO.:46), (SEQ. ID. NO.:51), (SEQ. ID. NO.:52), (SEQ. ID. NO.:55), (SEQ. ID. NO.:56), (SEQ. ID. NO.:57), (SEQ. ID. NO.:62), (SEQ. ID. NO.:63), (SEQ. ID. NO.:64), (SEQ. ID. NO.:73), (SEQ. ID. NO.:74), or (SEQ. ID. NO.:78); and

instructions for using the forward and reverse primers to detect a genetic predisposition in a human subject for non-responsiveness to treatment with a

statin drug selected from the group consisting of lovastatin, pravastatin, and simvastatin.

101. (Twice Amended) A genetic testing kit comprising:

a forward primer having a nucleotide sequence consisting of (SEQ. ID. NO.:82), (SEQ. ID. NO.:86), (SEQ. ID. NO.:88), (SEQ. ID. NO.:90), or (SEQ. ID. NO.:92);

a reverse primer having a nucleotide sequence consisting of (SEQ. ID. NO.:83), (SEQ. ID. NO.:84), (SEQ. ID. NO.:85), or (SEQ. ID. NO.:89); and

instructions for using the forward and reverse primers to detect a genetic predisposition in a human subject for non-responsiveness to treatment with a statin drug selected from the group consisting of lovastatin, pravastatin, and simvastatin.

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102. (Twice Amended) A genetic testing kit comprising:

a forward primer having a nucleotide sequence consisting of (SEQ. ID. NO.:95), (SEQ. ID. NO.:98), (SEQ. ID. NO.:99), (SEQ. ID. NO.:101), (SEQ. ID. NO.:102), (SEQ. ID. NO.:104), or (SEQ. ID. NO.:106);

a reverse primer having a nucleotide sequence consisting of (SEQ. ID. NO.:96), (SEQ. ID. NO.:97), (SEQ. ID. NO.:100), (SEQ. ID. NO.:103), or (SEQ. ID. NO.:105); and

instructions for using the forward and reverse primers to detect a genetic predisposition in a human subject for non-responsiveness to treatment with a statin drug selected from the group consisting of lovastatin, pravastatin, and simvastatin.

New Claims 103-117 are added as follows.

--103.(New) The oligonucleotide primer of Claim 84, wherein the primer is labeled with a fluorescent dye.

104.(New) The oligonucleotide primer of Claim 85, wherein the primer is labeled with a fluorescent dye.

105.(New) The oligonucleotide primer of Claim 86, wherein the primer is labeled with a fluorescent dye.

106.(New) The oligonucleotide primer of Claim 89, wherein the primer is labeled with a fluorescent dye.

107.(New) The oligonucleotide primer of Claim 91, wherein the primer is labeled with a fluorescent dye.

108.(New) The oligonucleotide primer set of Claim 92, wherein the forward primer or the reverse primer, or both, is labeled with a fluorescent dye.

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109.(New) The oligonucleotide primer set of Claim 93, wherein the forward primer or the reverse primer, or both, is labeled with a fluorescent dye.

110.(New) The oligonucleotide primer set of Claim 95, wherein the forward primer or the reverse primer, or both, is labeled with a fluorescent dye.

111.(New) The oligonucleotide primer set of Claim 96, wherein the forward primer or the reverse primer, or both, is labeled with a fluorescent dye.

112.(New) The genetic testing kit of Claim 97, wherein the primer is labeled with a fluorescent dye.

113.(New) The genetic testing kit of Claim 98, wherein the primer is labeled with a fluorescent dye.

114.(New) The genetic testing kit of Claim 99, wherein the primer is labeled with a fluorescent dye.

115.(New) The genetic testing kit of Claim 100, wherein the forward primer or the reverse primer, or both, is labeled with a fluorescent dye.

116.(New) The genetic testing kit of Claim 101, wherein the forward primer or the reverse primer, or both, is labeled with a fluorescent dye.

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117.(New) The genetic testing kit of Claim 102, wherein the forward primer or the reverse primer, or both, is labeled with a fluorescent dye.--.

REMARKS

The Pending Claims

Before entry of the preceding Amendment, Claims 82-86, 89, 91-93 and 95-102 are pending in the above-captioned application. Claims 82-86, 89, and 91 are directed to an oligonucleotide primer for detecting a genetic predisposition for non-responsiveness to statin drug treatment in a human. Claims 92-93 and 95-96 relate to an oligonucleotide primer set for detecting a genetic predisposition for non-responsiveness to statin drug treatment in a human. Claims 97-102 are directed to a genetic testing kit.

Applicant's Amendment

Applicant has added new Claims 103-117, support for which is found in the specification as originally filed, e.g., at page 14, line 34, through page 15, line 4.

Additional claim amendments to Claims 84-86, 89, 91-93, and 95-102, are described hereinbelow.

The Office Action and Applicant's Response

The Examiner stated that this application filed under former 37 CFR 1.60 lacks the necessary reference to the prior application and that the current status of all nonprovisional parent applications referenced should be included. In response, Applicant notes that in a Preliminary Amendment, filed together with the above-captioned application on July 3, 2001, Applicant inserted continuing data explaining the relationship to U.S. Serial No. 09/347,114, filed on July 2, 1999. Applicant has

herein updated the continuing data to mention that U.S. Serial No. 09/347,114 issued as U.S. Patent No. 6,297,014, on October 2, 2001.

The Examiner also stated that the title of the invention is not descriptive, and a new title is required that is clearly indicative of the invention to which the claims are directed. The Examiner suggested the following title: "Oligonucleotide primer sequences, primer sets and genetic testing kits for lipoprotein lipase gene." In response, Applicant has amended the title of the above-captioned application to "OLIGONUCLEOTIDE PRIMER SEQUENCES, PRIMER SETS, AND GENETIC TESTING KITS FOR LIPOPROTEIN LIPASE GENE ALLELES."

No claims were allowed.

The Examiner rejected Claims 97-102, under 35 U.S.C. § 112, second paragraph. The Examiner asserted that Claims 97-102 are indefinite over the recitation "the Nickerson reference sequence" or "the Oka reference sequence." In response, Applicant notes that the rejection has been overcome by the amendments to Claims 97-102 deleting these recitations. Therefore, Applicant respectfully requests the Examiner to withdraw the rejection of Claims 97-102 on this ground.

Claims 82-86, 89, 92-93, 95, 97-98, and 100-101 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 6-10, 13, 18-22, 26, 31-35, 38, 42, 46, 49-53 of U.S. Patent No. 6,297,014, which issued from the parent application of the above-captioned continuation application. The Examiner noted, *inter alia*, that "the instantly claimed primers were presented in the parent case and canceled without prejudice to pass the method claims to allowance. Thus, a restriction was never requested."

Applicant has herein canceled Claims 82 and 83, with respect to which the rejection is mooted. With respect to Claims 84-86, 89, 92-93, 95, 97-98, and 100-101, Applicant herewith submits a terminal disclaimer as to U.S. Patent No. 6,297,014.

The Examiner rejected Claims 82-86, 89, 91-93, and 95-102, under 35 U.S.C. § 103:

(i) Claim 98 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Gotoda (Journal of Lipid Res. Vol. 33, no. 7, pg. 1067-1072, 1992) in view of Stratagene (Catalog 1988). The Examiner stated the following reasons:

It is noted, with regard to the limitation that the kits contain instructions for detection of a predisposition for non-responsiveness to treatment with a statin drug, the inclusion of instructions is not considered to provide a patentable limitation on the claims because the instructions merely represent a statement of intended use in the form of instructions in a kit.

Gotoda et al. (herein referred to as Gotoda) teaches three DNA polymorphisms in the human lipoprotein lipase gene. Within intron 8, a T-G transversion occurs within a Hind II site. Gotoda also teaches Primer E and Primer F which function to amplify Intron 8. Primer E and Primer F and provided in Table 1 amplify intron 8. Primers C and D amplify intron 6. Primer D of Gotoda overlaps SEQ ID NO: 92 of the instant application. Primer D of Gotoda is located at positions 4641-4661. Primer of SEQ ID NO: 92 is located at positions 4647-4667. These primers share 14 nucleotides in common. Similarly, primers 82, 86, 88, 90 of the instant application overlap with Primer D of Gotoda.

Gotoda does not specifically teach a genetic testing kit with primers which overlap the sequences of SEQ ID NO: 82, 86, 88, 90 or 92 with respect to its position or Nickerson.

However, Stratagene teaches gene characterization kits which help explore identified gene. The kits provide reagents which have been assembled and pre-mixed and serve as a quality control. Further, the kits can save "weeks of costly and frustrating trouble-shooting".

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the primers Gotoda in kits as taught by Stratagene for the expected benefit of convenience and cost-effectiveness of practitioners in the art wishing to analyze intron 6 TTTA polymorphism of the lipase gene.

First, the Examiner stated that Primer D (i.e., 5′-CTTTAGACTC TTGTCCAGGT-3′) of the cited Gotoda *et al.* reference (see, Table 1, at page 1068) and SEQ ID NO: 92 of the above-captioned application "share 14 nucleotides in common" and that "primers 82, 86, 88, 90 of the instant application overlap with Primer D of Gotoda." The polynucleotide sequence of SEQ ID NO: 92 corresponds to nucleotide positions 4648-4667 of the Nickerson sequence (SEQ ID NO:80), i.e., 5′-ACAAGAGTCT AAAGCAGCAT-3′. Primer D appears to be *complementary* to nucleotide positions 4642-4661 of SEQ ID NO: 80, however, Applicant notes that SEQ ID NOS: 82, 86, 88, 90, and 92 are all forward primer sequences (see, Specification,at page 19, lines 22, 26, 28, 30, and 32), which single stranded oligonucleotide primer compounds Applicant asserts would have a different function and behave differently-- yielding different results in PCR amplification reactions-- compared to single stranded oligonucleotide primer compounds having *complementary* sequences.

Moreover, Applicant asserts that the basis of rejection is overcome by the amendment herein to Claim 98, to recite ". . . a primer having a nucleotide sequence *consisting of*" the designated nucleotide sequences, as chemical compounds distinct from the lipoprotein lipase gene, which primer sequences and the claimed genetic

testing kit containing them, the cited references failed to teach or suggest. Therefore, the Examiner is respectfully requested to withdraw the rejection on this ground.

Further, Claim 98 includes "instructions for using the primer to detect a genetic predisposition in a human subject for non-responsiveness to treatment with a statin drug selected from the group consisting of lovastatin, pravastatin, and simvastatin." The Examiner stated that the inclusion of instructions is not considered to provide a patentable limitation on the claims because the instructions merely represent a statement of intended use in the form of instructions in a kit. However, in numerous cases, including *In re Gulack*, 217 USPQ 401, 403 (CCPA 1983); *In re Lowry*, 32 USPQ2d 1031, 1033 (Fed. Cir. 1994), and *ex parte Carver*, 227 USPQ 465, 469 (BPAI 1985), the legal principal is well established that "printed matter may well constitute structural limitations upon which patentability can be predicated," in condideration of *all* the claim limitations taken as a whole. (*In re Gulack*, 217 USPQ, at 403, end of footnote 8).

(ii) Claims 97 and 98 were rejected under 35 U.S.C. 103(a) as being unpatentable over Zuliani *et al.* (Nucleic Acids Research, Vol. 18, no 16, pg. 4958, 1990) in view of Stratagene (Catalog 1988). The Examiner stated the following:

It is noted, with regard to the limitation that the kits contain instructions for detection of a predisposition for non-responsiveness to treatment with a statin drug, the inclusion of instructions is not considered to provide a patentable limitation on the claims because the instructions merely represent a statement of intended use in the form of instructions in a kit.

Zuilani teaches oligonucleotide primers which amplify intron 6 of the lipoprotein lipase gene which are identical to SEQ ID NO: 33 and SEQ ID NO: 34 (pg. 4958, Col. 2). The primers disclosed in Zuilani, 5'-ATCTGACAAGGATAGTGGGATATA-3' and 5'-CCTGGGTAACTGAGCGAGACTGTGTC-3' are 100% identical to the primers of the -instant claims. Additional SEQ ID NO: 87 and 91 of the instant application overlap the primers of Zuilani.

Zuliani does not specifically teach a genetic testing kit with primers of SEQ ID NO: 33 and 34, nor a genetic testing kit with primers which overlap SEQ ID NO: 87, 91.

However, Stratagene teaches gene characterization kits which help explore identified gene. The kits provide reagents which have been assembled and pre-mixed and serve as a quality control. Further, the kits can save "weeks of costly and frustrating trouble-shooting".

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the primers of Zuliani in kits as taught by Stratagene for the expected benefit of convenience and cost-effectiveness of practitioners in the art wishing to analyze intron 6 TTTA polymorphism of the lipase gene.

Claim 97 has been amended to delete the recitation of SEQ ID NOS: 33 and 34, and Claim 98 has been amended to delete the recitation of SEQ ID NOS: 87 and 91; Applicant asserts that the basis of rejection is further overcome by the

amendments to Claims 97 and 98, to recite ". . . a primer having a nucleotide sequence *consisting of*" the designated nucleotide sequences, as chemical compounds distinct from the lipoprotein lipase gene, which primer sequences and the claimed genetic testing kit containing them, the cited references failed to teach or suggest. Therefore, the Examiner is respectfully requested to withdraw the rejection on this ground.

Further, Claims 97 and 98 include "instructions for using the primer to detect a genetic predisposition in a human subject for non-responsiveness to treatment with a statin drug selected from the group consisting of lovastatin, pravastatin, and simvastatin." The Examiner stated that the inclusion of instructions is not considered to provide a patentable limitation on the claims because the instructions merely represent a statement of intended use in the form of instructions in a kit. However, in numerous cases, including *In re Gulack*, 217 USPQ 401, 403 (CCPA 1983); *In re Lowry*, 32 USPQ2d 1031, 1033 (Fed. Cir. 1994), and *ex parte Carver*, 227 USPQ 465, 469 (BPAI 1985), the legal principal is well established that "printed matter may well constitute structural limitations upon which patentability can be predicated," in condideration of *all* the claim limitations taken as a whole. (*In re Gulack*, 217 USPQ, at 403, end of footnote 8).

(iii) Claims 89 and 95 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glock et al (J. or Forensic Sciences, Vol. 41, no. 4, pg. 579-581, July 1996) or Takagi et al (Molecular and Cellular Probes, Vol. 10, pg. 227-228,1996) or Zuliani et al (Nucleic Acids Research, Vol. 18, no 16, pg. 4958, 1990) or Ahn (J. of Lipid Research, Vol. 34, pg. 421-428, 1993) in view of Nickerson (Nature Genetics, Vol. 19, no. 3, pg. 233-240, July 1999; Genbank Accession No. AF050163, September 1998).

This rejection encompasses oligonucleotides which amplify part of intron 6. "Consisting essentially of" language is read as open language indicating that the claims are drawn to sequences which contain the SEQ ID NO and any additional nucleotides on either side of the sequence. The intended use in the preamble of product claims carries no patentable weight.

Glock teaches oligonucleotide primers which amplify intron 6 of the lipoprotein lipase gene which are identical to SEQ ID NO: 33 and SEQ ID NO: 34 (pg. 579, col. 2, para. 3). The primers disclosed in Glock, 5'-ATCTGACAAGGATAGTGGGATATA-3' (forward primer- TTTA strand) and 5'-CCTGGGTAACTGAGCGAGACTGTGTC-3' (reverse primer-TAAA) are 100% identical to the primers of the instant claims. Additional SEQ ID NO: 87 and 91 of the instant application overlap these primers.

Takagi teaches oligonucleotide primers which amplify intron 6 of the lipoprotein lipase gene which are identical to SEQ ID NO: 37 and SEQ ID NO; 38 (pg. 227). The primers disclosed in Takagi, 5'-

ATCTGACAAGGATAGTGGGATATA-3' and 5'-CCTGGGTAACTGAGCGAGACTGTGTC-3' are 100% identical to the primers of the instant claims. Additional SEQ ID NO: 87 and 91 of the instant application overlap these primers.

Zuilani teaches oligonucleotide primers which amplify intron 6 of the lipoprotein lipase gene which are identical to SEQ ID NO: 37 and SEQ ID NO; 38 (pg. 4958, col. 2). The primers disclosed in Zuilani, 5'-ATCTGACAAGGATAGTGGGATATA-3' and 5'-CCTGGGTAACTGAGCGAGACTGTGTC-3' are 100% identical to the primers of the instant claims. Additional SEQ ID NO: 87 and 91 of the instant application overlap these primers.

Ahn teaches a primer pair which is designed to amplify a Pvull restriction site in intron 6. The primer pair of Ahn amplifies the newly identified TTTA repeat region.

Neither Glock, Takagi, Zuliani nor Ahn specifically teach all of the primer permutations of the instant claims.

However, Nickerson et al. (herein referred to as Nickerson) teaches the sequence of the human lipoprotein lipase gene. Nickerson also provides two positions for sequence variants within intron 6 of the sequence.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the primers of either Glock, Takagi, Ahn, or Zuliani with the teachings of Nickerson. Since the sequence of exon 6, intron 6, as well as the full length LPL gene, was known as provided by Nickerson, the ordinary artisan would have been motivated to amplify the region of intron 6 to detect the disclosed polymorphism. The TTTA polymorphism was known in the art at the time the invention was made. The ordinary artisan would have been motivated to have optimized primer selection within the intron around the TTTA polymorphism to obtain optimal results. Further, in the recent court decision In Re-Deuel 34 USPQ 2d 1210 (Fed. Cir. 1995), the court determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologues, however, the court stated

"Normally, a prima facie case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologues because homologues often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties."

Since the claimed primers simply represent functional equivalents of the primer pairs provided by Ahren, Takagi, Zuliani, or Glock, the ordinary artisan would have beer motivated to have obtained alternative primers, homologues, for amplification of the known polymorphism within intron 6. Any primer pairs which flank the known polymorphism would serve as functional equivalents of the known primer pairs which flank the polymorphism. Since the full length disclosed nucleic acid sequence of the LPL gene concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers are prima facie obvious over the cited reference in the absence of secondary considerations.

Contrary to the Examiner's assertion, Claim 89 and 95, even prior to the present amendment, do not recite SEQ ID NOS: 33 and 34. Claims 89 and 95 has been amended to delete the recitation of SEQ ID NOS: 87 and 91; Applicant asserts that the basis of rejection is further overcome by the amendment to Claims 89 and 95, to recite ". . . a primer having a nucleotide sequence *consisting of*" the designated nucleotide sequences, as chemical compounds distinct from the lipoprotein lipase gene, which primer sequences the cited references failed to teach or suggest.

Therefore, the Examiner is respectfully requested to withdraw the rejection on this ground.

(iv) Claims 82-86, 92-93 were rejected under 35 U.S.C. 103(a) as being unpatentable over Gotoda (Journal of Lipid Res. Vol. 33, no. 7, pg. 1067-1072,

1992) or Ahn (J. of Lipid Research, Vol. 34, pg. 421-428, 1993) in view of Nickerson (Nature Genetics, Vol 19, no. 3, pg. 233-240, July 1999; Genbank Accession No. AF050163, September 1998).

This rejection encompasses oligonucleotides which amplify intron 8 polymorphism HindIII. "Consisting essentially of language is read as open language indicating that the claims are drawn to sequences which contain the SEQ ID NO and any additional nucleotides on either side of the sequence. The intended use in the preamble of product claims carries no patentable weight.

Gotoda et al. (herein referred to as Gotoda) teaches three DNA polymorphisms in the human lipoprotein lipase gene. Within intron 8, a T-G transversion occurs within a Hind II site. Gotoda also teaches Primer E and Primer F which function to amplify Intron 8. Primer E and Primer F and provided in Table 1 amplify intron 8.

Ahn teaches forward and reverse primers for the explicit purpose of amplifying the sequence around a HindIII restriction site in intron 8. These primers are located in the regions flanking both the 5' and 3' end of the intron. The disclosed forward primer corresponds to nucleotides 7724-7744 and the reverse primer to nucleotides 8945-8963 of the Nickerson reference.

Neither Gotoda nor Ahn specifically teach all of the primer permutations of the instant claims.

However, Nickerson et al. (herein referred to as Nickerson) teaches the sequence of the human lipoprotein lipase gene. Nickerson also provides five sequence variants within intron 8 of the sequence.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the primers of Gotoda or Ahn 'with the teachings of Nickerson. Since the sequence of Intron 8, was known, the teachings in Nickerson and Gotoda of polymorphisms in intron 8 would have motivated the ordinary artisan to amplify the region of intron 8 flanking the HindIII polymorhpism. The ordinary artisan would have further been motivated to have optimized primer selection of intron to obtain optimal results. Further, in the recent court decision In Re Deuel 34 USPQ 2d 1210 (Fed. Cir. 1995), the court determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologues, however, the court stated

"Normally, a prima facie case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologues because homologues often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties."

Since the claimed primers simply represent functional equivalents of the primers of Gotoda and Ahn which amplify the HindIII polymorphism within intron 8. The art provides at least two pairs of primers which function to amplify the HindIII polymorphism, namely the primers of Gota E and F and the primers of Ahn. Any primer pairs which flank the known polymorphism would serve as functional equivalents of the known primer pairs which flank the polymorphism. The full length disclosed nucleic acid sequence of the LPL gene has been provided such that a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers are prima facie obvious over the cited reference in the absence of secondary considerations.

With respect to canceled Claims 82 and 83, the rejection is moot.

Contrary to the Examiner's comment, Claims 84 and 85, as originally filed, recited ". . . said primer *consisting of*" the designated sequence (SEQ ID NOS: 1 or 2), as chemical compounds distinct from the lipoprotein lipase gene, which primer sequences were not taught nor suggested by the cited references. Claims 84 and 85 are amended herein merely for greater clarity.

Further, Applicant submits that the basis of rejection is overcome by the amendments to Claims 86 and 92-93, to recite ". . . a primer having a nucleotide sequence *consisting of*" the designated nucleotide sequences, as chemical compounds distinct from the lipoprotein lipase gene, which primer sequences and

the primer sets containing them, were not taught nor suggested by the cited references.

Therefore, the Examiner is respectfully requested to withdraw the rejection on this ground.

(v) Claims 91 and 96 were rejected under 35 U.S.C. 103(a) as being unpatentable over Paulweber *et al.* (Atherosclerosis, Vol. 86, pg. 239-250, 1991) in view of Oka (Biochim. Biophys. Acta, Vol. 1049, no. 1, pg. 21-26, 1990; Genbank Accession No. X52978, November 1992).

This rejection encompasses oligonucleotides of the 3' UTR region, namely SEQ ID NO: 100-111. "Consisting essentially of language is read as open language indicating that the claims are drawn to sequences which contain the SEQ ID NO and any additional nucleotides on either side of the sequence. The intended use in the preamble of product claims carries no patentable weight.

Paulweber et al. (herein referred to as Paulweber) teaches several primers which are used to amplify the 3'UTR region of exon 10 (pg. 242, Figure 1). The position of the primers are provided in Table 2 (pg. 245)

Paulweber does not specifically teach the primer permutations of the instant claims.

However, Oka teaches the 3'UTR region and intron 10. Oka further teaches the gene sequence of exon 10 contains the entire 3''untranslated sequence and the potential polyadenylation sequences are 390 base pairs apart.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have designed primers, as taught by Paulweber, for the 3'UTR region, as taught by Oka, of the lipoprotein lipase gene. Since the sequence of the 3'UTR region was known, as taught by Oka, and the ordinary artisan would have been motivated to amplify the region of the 3'UTR region to detect the region, the gene, or to use the primer in combination with a primer at the most 5' region of the gene for amplification of the entire gene. The ordinary artisan would have further been motivated to have optimized primer selection within the region to obtain optimal results. Further, in the recent court decision In Re Deuel 34 USPQ 2d 1210 (Fed. Cir. 1995), the court determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologues, however, the court stated

"Normally, a prima facie case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologues because homologues often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties."

The claimed primers simply represent structural and functional homologues of the full length disclosed nucleic acid sequence of the LPL gene concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers are prima facie obvious over the cited reference in the absence of secondary considerations.

Applicant submits that the basis of rejection is overcome by the amendments to Claims 91 and 96, to recite ". . . a primer having a nucleotide sequence *consisting of*" the designated nucleotide sequences, which primer sequences (SEQ ID NO:95-106) as chemical compounds distinct from the lipoprotein lipase gene, were not taught nor suggested by the cited references.

Therefore, the Examiner is respectfully requested to withdraw the rejection on this ground.

(vi) Claims 97 and 100 were rejected under 35 U.S.C. 103(a) as being unpatentable over Gotoda (Journal of Lipid Res. Vol. 33, no. 7, pg. 1067-1072, 1992) or Ahn (J. of Lipid Research, Vol 34, pg. 421-428, 1993) in view of Nickerson (Nature Genetics, Vol. 19, no. 3, pg. 233-240, July 1999; Genbank Accession No. AF050163, September 1998) as applied to Claims 82-86, 92-93 above and further in view of Stratagene Catalog (1988).

It is noted, with regard to the limitation that the kits contain instructions for detection of a predisposition for non-responsiveness to treatment with a statin drug, the inclusion of instructions is not considered to provide a patentable limitation on the claims because the instructions merely represent a statement of intended use in the form of instructions in a kit.

Neither Nickerson, Gotoda nor Ahn specifically teach a genetic testing kit.

However, Stratagene teaches gene characterization kits which help explore identified gene. The kits provide reagents which have been assembled and pre-mixed and serve as a quality control. Further, the kits can save "weeks of costly and frustrating trouble-shooting".

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the primers of Gotoda or Ahn in view of Nickerson in kits as taught by Stratagene for the expected benefit of convenience and cost-effectiveness of practitioners in the art wishing to analyze intron f HindIII polymorphism of the lipase gene.

Applicant submits that the basis of rejection is overcome by the amendments to Claims 97 and 100, to recite ". . . a primer having a nucleotide sequence *consisting of*" the designated nucleotide sequences, which primer sequences as chemical compounds distinct from the lipoprotein lipase gene, were not taught nor suggested by the cited references. Therefore, the Examiner is respectfully requested to withdraw the rejection on this ground.

Further, Claims 97 and 100 include "instructions for using the primer to detect a genetic predisposition in a human subject for non-responsiveness to treatment with a statin drug selected from the group consisting of lovastatin, pravastatin, and simvastatin." The Examiner stated that the inclusion of instructions is not considered to provide a patentable limitation on the claims because the instructions merely represent a statement of intended use in the form of instructions in a kit. However, in numerous cases, including *In re Gulack*, 217 USPQ 401, 403 (CCPA 1983); *In re Lowry*, 32 USPQ2d 1031, 1033 (Fed. Cir. 1994), and *ex parte Carver*, 227 USPQ 465, 469 (BPAI 1985), the legal principal is well established that "printed matter may well constitute structural limitations upon which patentability can be predicated," in condideration of *all* the claim limitations taken as a whole. (*In re Gulack*, 217 USPQ, at 403, end of footnote 8).

(vii) Claims 98 and 101 were rejected under 35 U.S.C. 103(a) as being unpatentable over Glock *et al.* (J. or Forensic Sciences, Vol. 41, no. 4, pg. 579-581, July 1996) or Takagi *et al.* (Molecular and Cellular Probes, Vol. 10, pg. 227-228,1996) or Zuliani *et al.* (Nucleic Acids Research, Vol. 18, no 16, pg. 4958, 1990) or Ahn (J. of Lipid Research, Vol. 34, pg. 421-428, 1993) in view of Nickerson (Nature Genetics, Vol. 19, no. 3, pg. 233-240, July 1999; Genbank Accession No. AF050163, September 1998) as applied to Claims 89 and 95 above and further in view of Stratagene (1988).

It is noted, with regard to the limitation that the kits contain instructions for detection of a predisposition for non-responsiveness to treatment with a statin drug, the inclusion of instructions is not considered to provide a patentable limitation on the claims because the instructions merely represent a statement of intended use in the form of instructions in a kit.

Neither Nickerson, Glock, Takagi, Ahn nor Zuliani specifically teach a genetic testing kit.

However, Stratagene teaches gene characterization kits which help explore identified gene. The kits provide reagents which have been assembled and pre-mixed and serve as a quality control. Further, the kits can save "weeks of costly and frustrating trouble-shooting".

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the primers of Glock, Takagi, Ahn or Zuliani in kits as taught by Stratagene for the expected benefit of convenience and cost-effectiveness of practitioners in the art wishing to analyze intron 6 of the lipase gene.

Applicant submits that the basis of rejection is overcome by the amendments to Claim 98 and 101, to recite ". . . a primer having a nucleotide sequence *consisting of*" the designated nucleotide sequences, which designated primer sequences, as chemical compounds distinct from the lipoprotein lipase gene, were not taught nor suggested by the cited references. Therefore, the Examiner is respectfully requested to withdraw the rejection on this ground.

Further, Claims 98 and 101 include "instructions for using the primer to detect a genetic predisposition in a human subject for non-responsiveness to treatment with a statin drug selected from the group consisting of lovastatin, pravastatin, and simvastatin." The Examiner stated that the inclusion of instructions is not considered to provide a patentable limitation on the claims because the instructions merely represent a statement of intended use in the form of instructions in a kit. However, in numerous cases, including *In re Gulack*, 217 USPQ 401, 403 (CCPA 1983); *In re Lowry*, 32 USPQ2d 1031, 1033 (Fed. Cir. 1994), and *ex parte Carver*, 227 USPQ 465, 469 (BPAI 1985), the legal principal is well established that "printed matter may well constitute structural limitations upon which patentability

can be predicated," in condideration of *all* the claim limitations taken as a whole. (*In re Gulack*, 217 USPQ, at 403, end of footnote 8).

(viii) Claims 99 and 102 were rejected under 35 U.S.C. 103(a) as being unpatentable over Paulweber et al (Artherosclerosis, Vol. 86, pg. 239-250, 1991) in view of Oka (Biochim. Biophys. Acta, Vol. 1049, no. 1, pg. 21-26, 1990; Genbank Accession No. X52978, November 1992) as applied to Claims 91 and 96 above and further in view of Stratagene Catalog (1988).

It is noted, with regard to the limitation that the kits contain instructions for detection of a predisposition for non-responsiveness to treatment with a statin drug, the inclusion of instructions is not considered to provide a patentable limitation on the claims because the instructions merely represent a statement of intended use in the form of instructions in a kit.

Neither Oka nor Paulweber specifically teaches a genetic testing kit.

However, Stratagene teaches gene characterization kits which help explore identified gene. The kits provide reagents which have been assembled and pre-mixed and serve as a quality control. Further, the kits can save "weeks of costly and frustrating trouble-shooting".

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the primers of Oka and Paulweber in kits as taught by Stratagene for the expected benefit of convenience and cost-effectiveness of practitioners in the art wishing to analyze the 3'-UTR region of the lipase gene.

Applicant submits that the basis of rejection is overcome by the amendments to Claims 99 and 102, to recite ". . . a primer having a nucleotide sequence *consisting of*" the designated nucleotide sequences, which primer sequences (SEQ ID NO:95-106), as chemical compounds distinct from the lipoprotein lipase gene, were not taught nor suggested by the cited references. Therefore, the Examiner is respectfully requested to withdraw the rejection on this ground.

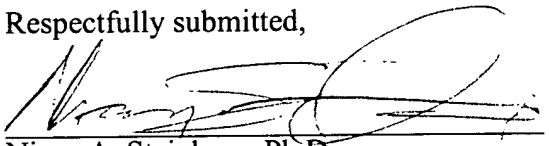
Further, Claims 99 and 102 include "instructions for using the primer to detect a genetic predisposition in a human subject for non-responsiveness to treatment with a statin drug selected from the group consisting of lovastatin, pravastatin, and simvastatin." The Examiner stated that the inclusion of instructions is not considered to provide a patentable limitation on the claims because the instructions merely represent a statement of intended use in the form of instructions in a kit. However, in numerous cases, including *In re Gulack*, 217 USPQ 401, 403 (CCPA 1983); *In re Lowry*, 32 USPQ2d 1031, 1033 (Fed. Cir. 1994), and *ex parte Carver*, 227 USPQ 465, 469 (BPAI 1985), the legal principal is well established that "printed matter may well constitute structural limitations upon which patentability

can be predicated," in condideration of *all* the claim limitations taken as a whole. (*In re Gulack*, 217 USPQ, at 403, end of footnote 8).

CONCLUSION

In view of the above amendments and remarks, it is submitted that this application is now ready for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney at (213) 896-6665.

Respectfully submitted,



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